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Cycloaddition of nitrones with arynes generated from benzobisoxadisilole or 2,3-naphthoxadisilole

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ABSTRACT

1,3-Dipolar cycloaddition of nitrones with arynes generated in situ from benzobisoxadisilole or 2,3-naphthoxadisilole afforded the oxadisilole fused benzo[*d*]isoxazoline or the naphtho[2,3-*d*]isoxazoline derivatives at room temperature in good yields.

1. Introduction

Benzoisoxazolidine derivatives are important heterocycle compounds. They have been widely used as the building blocks of bioactive substances, intermediate of chiral pharmaceuticals and natural products.[1] 1,3-Dipolar cycloaddition is one of the most useful methods for synthesizing heterocycles.[2] However, only few examples are reported in the literatures on the 1,3-dipolar cycloaddition of nitrones with arynes.[1a,3] Aryne is an important intermediate and synthon in organic synthesis.[4] Recently, we explored the aryne generation chemistry from benzobisoxadisiloles, benzotrisoxadisilole, and 2,3-naphthoxadisilole. We found that benzobisoxadisiloles can serve as the synthetic equivalents of benzdiyne.[5] The chemistry was further extended to the synthesis and isolation of oxadisilole fused isobenzofurans and isoindoles, and their applications in the preparation of functional acenes and benzoquinones.[6] With this motif in mind, herein, we describe the 1,3-dipolar cycloaddition reaction of nitrones with arynes generated in situ from benzobisoxadisilole or 2,3-naphthoxadisilole. Oxadisilole fused benzo[*d*]isoxazoline or naphtho[2,3-*d*]isoxazoline derivatives were obtained in good yields under very mild reaction conditions.

2. Results and discussion

The preparation of the oxadisilole fused benzo[*d*]isoxazoline derivatives **5a**–**g** or the naphtho[2,3-*d*]isoxazoline **9a**–**e** are outlined in Schemes 1 and 3. Arynes **3** and **8** were generated from benzobisoxadisilole **1** and 2,3-naphthoxadisilole **6**, respectively through our previously reported phenyliodination fluoride induced desilylation protocol.[5] Trapping benzyne **3** and naphthyne **8** at room temperature with nitrons **4a**–**g** via 1,3-dipolar cycloaddition reactions afforded the oxadisilole fused benzo[*d*]isoxazoline derivatives **5a**–**g** and naphtho[2,3-*d*]isoxazoline **9a**–**e** in good yields. Nitrones **4a**–**g** were prepared according to the literature procedures.[7,8]

In situ phenyliodination of **1** with a 1.5:3 mixture of phenyliodium diacetate ($PhI(OAc)_2$) and trifluoromethanesulfonic acid (TfOH) took place readily at room temperature in CH_2Cl_2 (Scheme 1). Without isolation of the ring-opened iodination intermediate **2**, benzyne **3** could be generated in situ upon treatment with a 1.0 M THF solution of tetrabutylammonium fluoride (n-Bu_4NF). Trapping experiments were carried out with 5 equiv of nitrone **4c** (X=H) at room temperature to afford 68% isolated yields of the oxadisilole fused benzo[*d*]isoxazoline derivative **5c** in this three steps reaction (Scheme 1 and Table 1, entry 4). We also observed that using less than 5 equivalents of nitrone **4c**, the yields were decreased (Table 1, entries 1–3). However, increased the amount to 10 equivalents, the yield of **5c** was not improved (Table 1, entry 5). If CH_3CN was used as solvent (commonly used in preparing precursor, [*o*-(trimethyl) phenyl]-iodonium triflate),[9] the 1,3-dipolar cycloaddition reaction

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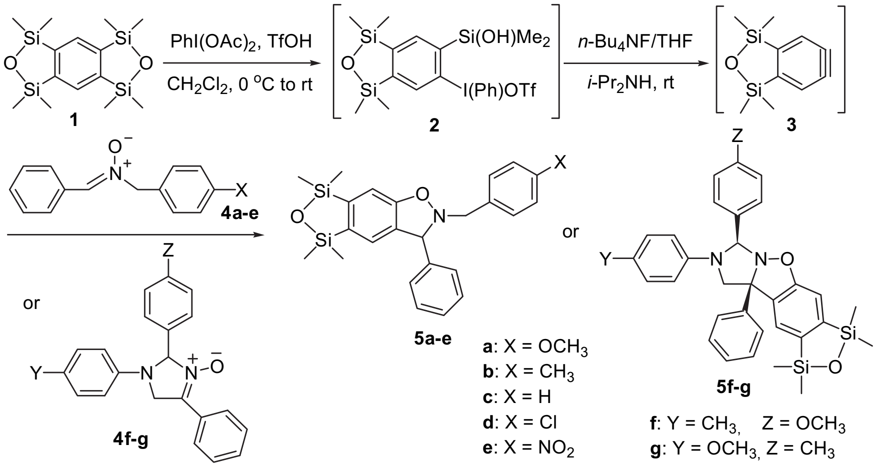
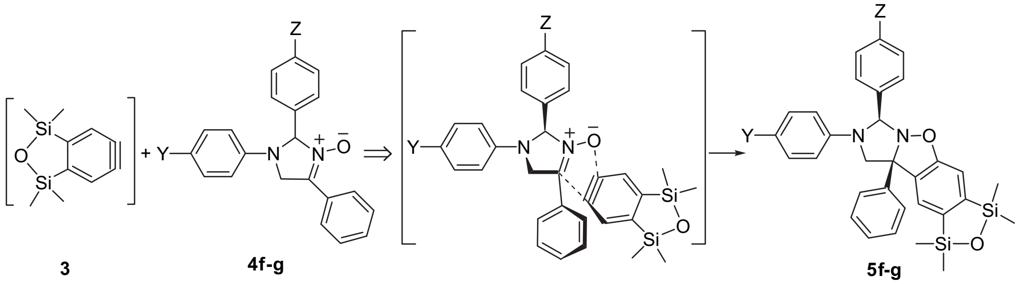
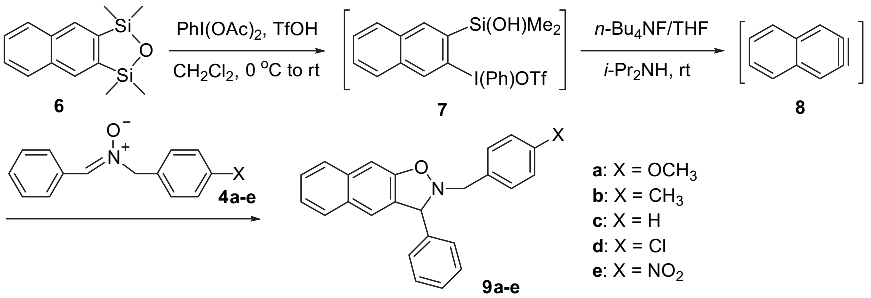


Scheme 1.



Scheme 2.



Scheme 3.

of benzyne **3** with nitron **4c** was unsuccessful. It is worth noting that the remaining material **4c** could be recycled.

We further studied the 1,3-dipolar cycloaddition reaction of benzyne **3** generated in situ from the benzobisoxadisilole **1** with various nitrones **4a**–**e** at room temperature. The oxadisilole fused benzo[*d*]isoxazoline derivatives **5a**–**e** were formed in 50–78% yields (Scheme 1 and Table 2, entries 1–5). As shown from the chemical yields, this 1,3-dipolar cycloaddition of nitrone to benzyne **3** is rather insensitive in the electronic nature (X=OCH_3, CH_3, H, Cl, NO_2) of the substituents on the nitrones. For cyclic nitrones **4f**–**g**, the *cis* cycloadducts **5f**–**g** could be obtained in 30–35% yields, the phenyl and aryl group were on the same side of the benzobicyclic ring system (Scheme 1 and Table 3, entries 1 and 2). The possible reaction mechanism shown in Scheme 2 would account for the high stereoselectivity. The fact that only *cis* isomer was obtained demonstrated that the reaction was a concerted process guided with the Woodward–Hoffman rule. When the molecule of benzyne **3** approaches planar dipole *N*-oxide **4f**–**g**, the concerted reaction prefers to approach the dipole from the less sterically hindered side of the plane and thus afforded *cis* iomers **5f**–**g**.[8b,10] As compared with the acyclic nitrones **4a**–**e**, the cycloadducts **5f**–**g**

Table 1
Cycloaddition of nitrone **4c** with benzyne **3** generated from benzobisoxadisilole **1** at room temperature

Entry	Molar ratio of **1** to **4c**	Yield[a] of **5c** (%)
1	1:1	30
2	1:2	54
3	1:3	55
4	1:5	68
5	1:10	65

[a] Isolated yields.

Table 2
Cycloaddition of nitrones **4a**–**e** with benzyne **3** generated from benzobisoxadisilole **1** at room temperature

Entry	Nitrone	X	Product	Yield[a] (%)
1	**4a**	OCH_3	**5a**	50
2	**4b**	CH_3	**5b**	78
3	**4c**	H	**5c**	68
4	**4d**	Cl	**5d**	61
5	**4e**	NO_2	**5e**	61

[a] Isolated yields.

Table 3
Cycloaddition of nitrones **4f**–**g** with benzyne **3** generated from benzobisoxadisilole **1** at room temperature

Entry	Nitrone	Y	Z	Product	Yield[a] (%)
1	**4f**	CH_3	OCH_3	**5f**	35
2	**4g**	OCH_3	CH_3	**5g**	30

[a] Isolated yields.

were formed in lower yields. It may be due to the steric effects. The structures of compounds **5f**–**g** are interesting for synthesizing heterocycles.

Furthermore, 1,3-dipolar cycloaddition reactions of naphthyne **8** generated in situ from the 2,3-naphthoxadisilole **6** with various nitrones **4a**–**e** at room temperature were also investigated. The naphtho[2,3-*d*]isoxazoline derivatives **9a**–**e** were formed in good yields (Scheme 3 and Table 4, entries 1–5). The structures of all the cycloadducts **5a**–**g** and **9a**–**e**, were established by ^1H and ^{13}C NMR, MS, IR, elemental analysis and HRMS.

Table 4
Cycloaddition of nitrones **4a**–**e** with 2,3-naphthyne **8** generated from 2,3-naphthoxadisilole **6** at room temperature

Entry	Nitrone	X	Product	Yield[a] (%)
1	**4a**	OCH_3	**9a**	81
2	**4b**	CH_3	**9b**	66
3	**4c**	H	**9c**	84
4	**4d**	Cl	**9d**	73
5	**4e**	NO_2	**9e**	76

[a] Isolated yields.

In conclusion, we have investigated 1,3-dipolar cycloaddition of nitrones **4a**–**g** with arynes **3** and **8** generated in situ from the benzobisoxadisilole **1** or 2,3-naphthoxadisilole **6**, respectively. Oxadisilole fused benzo[*d*]isoxazoline **5a**–**g** and naphtho[2,3-*d*]isoxazoline derivatives **9a**–**e** were synthesized in good yields under very mild reaction conditions. The simplicity of these procedures and good yields should offer great opportunities for the synthesis of important heterocyclic compounds.

3. Experimental

3.1. General

All non-aqueous reactions were carried out in oven-dried glassware under a slight positive pressure of nitrogen unless otherwise noted. All reagents and solvents were obtained from commercial sources and used without purification, unless indicated otherwise. Solvents were reagent grade and purified by standard techniques: THF was distilled from Na-benzophenone; CH_2Cl_2 was distilled from CaH_2. Melting points were determined on a WRS-1 digital melting point apparatus and are uncorrected. IR spectra were determined on a Bruker spectrometer and expressed in cm^{-1} (KBr disc). NMR spectra were recorded on a Bruker DRX-500 NMR spectrometer (500 MHz for ^1H and 125 MHz for ^{13}C) with $CDCl_3$ as the solvent and TMS as internal reference and expressed in ppm. Coupling constants (*J*) are reported in Hertz. Low-resolution mass spectra were obtained on a Agilent LC/MSD SL spectrometer in EI mode and reported as *m*/*z*. High-resolution mass spectra (HRMS) were recorded on a Waters Micromass GCT instrument. Elemental analyses were measured on the Elemental Vario EL III. Column chromatography was performed using silica gel (G or GF_{254}). PE indicates petroleum ether (bp 60–80 °C).

3.2. General procedure for the preparation of nitrones

3.2.1. General procedure for the preparation of nitrones ***4a*–*e***[7]. A mixture of *p*-substituted benzaldehyde (0.02 mol) and hydroxylamine hydrochloride (2.07 g, 0.03 mol) in 15 mL of MeOH was stirred for 1 h, then the solvent was evaporated and the residue was extracted with ethyl acetate (25 mL×3). The combined organic phase was dried over anhydrous $MgSO_4$, filtered and evaporated. The crude *p*-substituted benzaldehyde oxime was used without further purification.

To a solution of *p*-substituted benzaldehyde oxime (10.0 mmol) and $NaBH_3CN$ (1.07 g, 17.0 mmol) in 10 mL of MeOH was added a trace of bromocresol green as an indicator. Concentrated HCl was then added dropwise with stirring to maintain a yellow color (pH ~ 4). The reaction mixture was stirred at room temperature for 24 h. The mixture was then made basic with 10% NaOH and it was extracted with CH_2Cl_2. The organic layer was dried over anhydrous $MgSO_4$, the solvent was evaporated, and the solid residue *N*-(*p*-substituted benzyl)hydroxylamine was obtained.

To a stirred solution of *N*-(*p*-substituted benzyl)hydroxylamine (5 mmol) in 3 mL of CH_2Cl_2 was treated with benzaldehyde (0.8 mL, 7.5 mmol) and anhydrous $MgSO_4$ (1.2 g, 10.0 mmol). The mixture was vigorously stirred at room temperature for overnight, the reaction mixture was filtered and the filtrate evaporated under reduced pressure, the residue was purified by column chromatography on silica gel using a gradient of 10–20% EtOAc in petroleum ether (60–80 °C) as eluent to afford the nitrones **4a**–**e**.

3.2.2. General procedure for the preparation of nitrones ***4f*–*g***[8]. A mixture of *α*-bromoacetophenone (3.96 g, 0.02 mol) and hydroxyl amine hydrochloride (2.07 g, 0.03 mol) in 15 mL of MeOH was stirred for 1 h, then the solvent was evaporated and the residue was extracted with ethyl acetate (25 mL×3). The combined organic phase was dried over anhydrous $MgSO_4$, filtered and evaporated. The crude *α*-bromoacetophenone oxime was used without further purification.

The solid *α*-bromoacetophenone oxime (2.5 mmol) was added to a solution of aromatic amine (5.0 mmol) in 10 mL of absolute ethanol and the mixture was stirred for 20 min followed by adding aromatic aldehyde (5.0 mmol) and then stirred for 3 h at room temperature. The formed precipitate was collected by filtration and recrystallized from acetone to get cycloadducts **4f**–**g**.

3.3. General procedure for the preparation of oxadisilole fused benzo[*d*]isoxazoline derivatives 5a–g and naphtho [2,3-*d*]isoxazoline 9a–e

Trifluoromethanesulfonic acid (0.27 mL, 3.0 mmol) was added with a syringe to a stirred solution of phenyliodium diacetate (493 mg, 1.5 mmol in 10 mL of CH_2Cl_2) at 0 °C. The mixture was stirred under N_2 for 1 h at 0 °C and for 2 h at room temperature. The clear yellow solution was cooled again to 0 °C followed by dropwise addition of a cold (0 °C) solution of the benzobisoxadisilole **1** (or 2,3-naphthoxadisilole **6**) (1.0 mmol in 5 mL of CH_2Cl_2). The mixture was stirred for 0.5 h at 0 °C and warmed up to room temperature. After benzobisoxadisilole **1** (or 2,3-naphthoxadisilole **6**) disappeared (monitored by TLC), diisopropylamine (0.35 mL, 2.5 mmol) and nitrones **4** (5.0 mmol) were added followed by a solution of tetrabutylammonium fluoride (2.5 mL, 2.5 mmol, 1.0 M solution in THF). The mixture was stirred under N_2 for 5 h at room temperature. The organic solvent was removed under reduced pressure. The crude product was purified by column chromatography on silica gel using a gradient of 2–5% EtOAc in petroleum ether (60–80 °C) as eluent to afford cycloadducts **5a**–**g** and **9a**–**e**.

*3.3.1. 2-(4-Methoxybenzyl)-3-phenyl-5,6-oxadisilole fused benzo [d] isoxazolidine (**5a**).* As a white solid; mp 94–95 °C; ^{1}H NMR (500 MHz, CDCl$_3$) δ 0.27 (s, 3H), 0.31 (s, 3H), 0.33 (s, 3H), 0.35 (s, 3H), 3.81 (s, 3H), 4.10 (d, J=13.5 Hz, 1H), 4.32 (d, J=13.0 Hz, 1H), 5.33 (s, 1H), 6.87 (d, J=8.5 Hz, 2H), 7.00 (s, 1H), 7.16 (s, 1H), 7.29–7.35 (m, 7H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 1.05, 1.12, 1.4, 1.5, 55.4, 62.1, 72.3, 110.0, 113.9, 126.9, 127.97, 128.04, 128.3, 128.7, 130.7, 131.2, 140.2, 140.5, 150.0, 157.6, 159.2; IR (KBr) 2957, 1612, 1556, 1514, 1450, 1251, 1097, 930, 844 cm^{-1}; MS m/z (%) (EI): 447 (M$^+$, 18), 326 (16), 311 (13), 121 (100); Anal. Calcd for $C_{25}H_{29}NO_3Si_2$: C, 67.07; H, 6.53; N, 3.13. Found: C, 67.28; H, 6.63; N, 3.10.

*3.3.2. 2-(4-Methylbenzyl)-3-phenyl-5,6-oxadisilole fused benzo [d] isoxazolidine (**5b**).* As a white solid; mp 102–103 °C; ^{1}H NMR (500 MHz, CDCl$_3$) δ 0.27 (s, 3H), 0.31 (s, 3H), 0.33 (s, 3H), 0.35 (s, 3H), 2.34 (s, 3H), 4.13 (d, J=13.5 Hz, 1H), 4.33 (d, J=13.5 Hz, 1H), 5.33 (s, 1H), 6.99 (d, J=0.5 Hz, 1H), 7.14–7.17 (m, 3H), 7.29–7.34 (m, 7H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 1.05, 1.12, 1.4, 1.5, 21.3, 62.5, 72.4, 110.1, 126.9, 128.0, 128.1, 128.8, 129.2, 129.4, 131.2, 133.3, 137.4, 140.2, 140.5, 150.0, 157.7; IR (KBr) 2958, 1600, 1556, 1515, 1450, 1252, 1097, 930, 844 cm^{-1}; MS m/z (%) (EI): 431 (M$^+$, 51), 354 (9), 326 (100), 311 (31); Anal. Calcd for $C_{25}H_{29}NO_2Si_2$: C, 69.56; H, 6.77; N, 3.24. Found: C, 69.54; H, 6.74; N, 3.12.

*3.3.3. 2-Benzyl-3-phenyl-5,6-oxadisilole fused benzo [d] isoxazolidine (**5c**).* As a white solid; mp 101–102 °C; ^{1}H NMR (500 MHz, CDCl$_3$) δ 0.27 (s, 3H), 0.31 (s, 3H), 0.33 (s, 3H), 0.35 (s, 3H), 4.17 (d, J=13.5 Hz, 1H), 4.38 (d, J=13.5 Hz, 1H), 5.34 (s, 1H), 7.00 (d, J=0.5 Hz, 1H), 7.18 (d, J=1.0 Hz, 1H), 7.25–7.33 (m, 8H), 7.33–7.40 (m, 2H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 1.06, 1.13, 1.4, 1.5, 62.8, 72.7, 110.1, 126.9, 127.8, 128.0, 128.1, 128.6, 128.8, 129.4, 131.2, 136.4, 140.3, 140.4, 150.1, 157.6; IR (KBr) 2957, 1600, 1556, 1494, 1450, 1252, 1097, 930, 842 cm^{-1}; MS m/z (%) (EI): 417 (M$^+$, 59), 340 (31), 326 (100), 313 (35); Anal. Calcd for $C_{24}H_{27}NO_2Si_2$: C, 69.02; H, 6.52; N, 3.35. Found: C, 68.77; H, 6.68; N, 3.19.

*3.3.4. 2-(4-Chlorobenzyl)-3-phenyl-5,6-oxadisilole fused benzo [d] isoxazolidine (**5d**).* As a white solid; mp 96–97 °C; ^{1}H NMR (500 MHz, CDCl$_3$) δ 0.27 (s, 3H), 0.30 (s, 3H), 0.33 (s, 3H), 0.34 (s, 3H), 4.27 (d, J=14.5 Hz, 1H), 4.42 (d, J=14.5 Hz, 1H), 5.35 (s, 1H), 6.97 (d, J=0.5 Hz, 1H), 7.15 (s, 1H), 7.35–7.43 (m, 5H), 7.60 (d, J=8.5 Hz, 2H), 8.20 (d, J=8.5 Hz, 2H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 1.05, 1.11, 1.4, 1.5, 62.0, 73.0, 110.1, 126.8, 128.0, 128.3, 128.7, 128.9, 130.6, 131.1, 133.6, 135.1, 140.1, 140.5, 150.2, 157.4; IR (KBr) 2957, 1599, 1557, 1492, 1448, 1252, 1097, 934, 841 cm^{-1}; MS m/z (%) (EI): 451 (M$^+$, 43), 374 (20), 326 (100), 311 (29); Anal. Calcd for $C_{24}H_{26}ClNO_2Si_2$: C, 63.76; H, 5.80; N, 3.10. Found: C, 63.44; H, 5.88; N, 2.93.

*3.3.5. 2-(4-Nitrobenzyl)-3-phenyl-5,6-oxadisilole fused benzo [d] isoxazolidine (**5e**).* As a white solid; mp 144–145 °C; ^{1}H NMR (500 MHz, CDCl$_3$) δ 0.28 (s, 3H), 0.32 (s, 3H), 0.34 (s, 3H), 0.36 (s, 3H), 4.28 (d, J=14.5 Hz, 1H), 4.43 (d, J=14.5 Hz, 1H), 5.37 (s, 1H), 6.98 (s, 1H), 7.17 (s, 1H), 7.34–7.45 (m, 5H), 7.61 (d, J=9.0 Hz, 2H), 8.19–8.21 (m, 2H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 1.2, 1.3, 1.6, 1.7, 62.0, 74.0, 110.1, 123.9, 126.9, 128.3, 128.8, 129.2, 129.9, 131.3, 139.8, 141.0, 144.6, 147.7, 150.6, 157.3; IR (KBr) 2955, 1604, 1556, 1521, 1450, 1346, 1252, 1100, 927, 841 cm^{-1}; MS m/z (%) (EI): 462.2 (M$^+$, 81), 385.2 (82), 326.2 (100), 311.1 (60); Anal. Calcd for $C_{24}H_{26}N_2O_4Si_2$: C, 62.31; H, 5.66; N, 6.06; Found: C, 62.07; H, 5.69; N, 6.02.

*3.3.6. Cycloadduct **5f** from cycloaddition of nitrone **4f** with benzyne **3** generated from benzobisoxadisilole **1**.* As a white solid; mp 138–140 °C; ^{1}H NMR (500 MHz, CDCl$_3$) δ 0.32 (s, 3H), 0.33 (s, 3H), 0.360 (s, 3H), 0.364 (s, 3H), 2.2 (s, 3H), 3.77 (s, 3H), 4.37 (d, J=9.5 Hz, 1H), 4.42 (d, J=9.5 Hz, 1H), 5.75 (s, 1H), 6.49 (d, J=8.5 Hz, 2H), 6.82–6.84 (m, 2H), 6.94 (d, J=8.5 Hz, 2H), 7.02 (s, 1H), 7.23–7.24 (m, 1H), 7.29–7.32 (m, 2H), 7.36–7.38 (m, 2H), 7.43 (s, 1H), 7.56–7.58 (m, 2H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 1.08, 1.16, 1.51, 1.53, 21.2, 55.3, 61.0, 77.7, 86.3, 110.6, 114.0, 114.4, 125.98, 126.03, 127.4, 127.6, 128.6, 128.9, 129.6, 130.9, 133.8, 141.1, 142.4, 143.6, 150.5, 157.3, 159.6; IR (KBr) 2952, 1614, 1516, 1253, 1103, 1036, 930, 845 cm^{-1}; HRMS: m/z [M]$^+$ calcd for $C_{33}H_{36}N_2O_3Si_2$: 564.2265; found 564.2263.

*3.3.7. Cycloadduct **5g** from cycloaddition of nitrone **4g** with benzyne **3** generated from benzobisoxadisilole **1**.* As a white solid; mp 138–139 °C; ^{1}H NMR (500 MHz, CDCl$_3$) δ 0.30 (s, 3H), 0.31 (s, 3H), 0.346 (s, 3H), 0.353 (s, 3H), 2.30 (s, 3H), 3.65 (s, 3H), 4.30 (d, J=9.5 Hz, 1H), 4.41 (d, J=9.5 Hz, 1H), 5.64 (s, 1H), 6.52–6.54 (m, 2H), 6.68 (d, J=9.5 Hz, 2H), 7.02 (d, J=0.5 Hz, 1H), 7.09 (d, J=8.0 Hz, 2H), 7.21–7.23 (m, 1H), 7.28–7.31 (m, 2H), 7.34 (d, J=8.0 Hz, 2H), 7.45 (d, J=0.5 Hz, 1H), 7.57–7.59 (m, 2H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 0.98, 1.05, 1.46, 1.49, 21.1, 55.6, 62.0, 77.5, 87.0, 110.6, 114.5, 116.1, 125.98, 126.05, 127.5, 127.7, 128.6, 129.3, 133.8, 135.9, 138.1, 140.1, 141.1, 142.7, 150.4, 152.7, 157.4; IR (KBr) 2955, 1617, 1512, 1249, 1102, 1040, 930, 791 cm^{-1}; HRMS: m/z [M]$^+$ calcd for $C_{33}H_{36}N_2O_3Si_2$: 564.2265; found 564.2261.

*3.3.8. 2-(4-Methoxybenzyl)-3-phenyl naphtho [2,3-d] isoxazolidine (**9a**).* As a white solid; mp 120–121 °C; ^{1}H NMR (500 MHz, CDCl$_3$) δ 3.81 (s, 3H), 4.14 (d, J=13.0 Hz, 1H), 4.35 (d, J=13.0 Hz, 1H), 5.42 (s, 1H), 6.88–6.90 (m, 2H), 7.16 (s, 1H), 7.28–7.45 (m, 10H), 7.67–7.73 (m, 2H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 55.4, 62.0, 72.0, 102.8, 114.0, 123.5, 123.8, 126.5, 127.2, 128.1, 128.2, 128.3, 128.8, 130.0, 130.8, 132.7, 134.8, 140.1, 155.1, 159.3; IR (KBr) 3059, 2831, 1639, 1512, 1448, 1247, 1091, 1037 cm^{-1}; HRMS: m/z [M]$^+$ calcd for $C_{25}H_{21}NO_2$: 367.1572; found 367.1570.

*3.3.9. 2-(4-Methylbenzyl)-3-phenyl naphtho [2,3-d] isoxazolidine (**9b**).* As a white solid; mp 131–132 °C; ^{1}H NMR (500 MHz, CDCl$_3$) δ 2.40 (s, 3H), 4.21 (d, J=13.5 Hz, 1H), 4.40 (d, J=13.5 Hz, 1H), 5.46 (s, 1H), 7.21 (d, J=8.0 Hz, 2H), 7.32–7.49 (m, 11H), 7.71–7.77 (m, 2H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 21.3, 62.3, 72.1, 102.8, 123.4, 123.7, 126.4 127.2, 128.0, 128.1, 128.2, 128.8, 129.3, 129.4, 130.0, 132.7, 133.3, 134.7, 137.5, 140.0, 155.1; IR (KBr) 3037, 2856, 2830, 1634, 1506, 1452, 1253, 1232, 1213, 1162, 1080 cm^{-1}; MS m/z (%) (EI): 351 (M$^+$, 49), 246 (24), 231 (100), 202 (18); Anal. Calcd for $C_{25}H_{21}NO$: C, 85.44; H, 6.02; N, 3.99; Found: C, 85.38; H, 6.04; N, 3.97.

*3.3.10. 2-Benzyl-3-phenyl naphtho [2,3-d] isoxazolidine (**9c**).* As a white solid; mp 126–127 °C; ^{1}H NMR (500 MHz, CDCl$_3$) δ 4.22 (d, J=13.5 Hz, 1H), 4.42 (d, J=13.5 Hz, 1H), 5.44 (s, 1H), 7.17 (s, 1H), 7.29–7.46 (m, 13H), 7.68–7.74 (m, 2H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 62.6, 72.4, 102.8, 123.4, 123.8, 126.5, 127.2, 127.9, 128.1, 128.2, 128.3, 128.6, 128.8, 129.4, 130.0, 132.7, 134.7, 136.4, 139.9, 155.0; IR (KBr) 3036, 2919, 1635, 1495, 1455, 1252, 1164, 1093 cm^{-1}; MS m/z (%) (EI): 337 (M$^+$, 62), 246 (44), 231 (100), 202 (25); Anal. Calcd for $C_{24}H_{19}NO$: C, 85.43; H, 5.68; N, 4.15; Found: C, 85.54; H, 5.69; N, 3.86.

*3.3.11. 2-(4-Chlorobenzyl)-3-phenyl naphtho [2,3-d] isoxazolidine (**9d**).* As a white solid; mp 138–139 °C; ^{1}H NMR (500 MHz, CDCl$_3$) δ 4.18 (d, J=13.5 Hz, 1H), 4.34 (d, J=13.5 Hz, 1H), 5.41 (s, 1H), 7.16

(s, 1H), 7.29–7.44 (m, 12H), 7.69–7.74 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 61.8, 72.8, 102.8, 123.4, 123.9, 126.6, 127.2, 128.1, 128.2, 128.4, 128.8, 128.9, 130.1, 130.7, 132.6, 133.7, 134.7, 135.0, 139.6, 154.8; IR (KBr) 3062, 2881, 1640, 1507, 1492, 1447, 1246, 1089, 1015 cm^{-1}; MS m/z (%) (EI): 371 (M^+, 43), 231 (100), 246 (41), 202 (21); Anal. Calcd for $C_{24}H_{18}ClNO$: C, 77.52; H, 4.88; N, 3.77; Found: C, 77.70; H, 4.78; N, 3.52.

*3.3.12. 2-(4-Nitrobenzyl)-3-phenyl naphtho [2,3-d] isoxazolidine (**9e**).* As a white solid; mp 140–141 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.31 (d, J=14.0 Hz, 1H), 4.44 (d, J=14.0 Hz, 1H), 5.45 (s, 1H), 7.13 (s, 1H), 7.30–7.46 (m, 8H), 7.63 (d, J=8.5 Hz, 2H), 7.69 (d, J=8.5 Hz, 1H), 7.72 (d, J=8.5, 1H), 8.22 (d, J=8.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 61.7, 73.6, 102.8, 123.4, 123.8, 124.1, 126.7, 127.3, 128.1, 128.3, 128.7, 129.1, 129.8, 130.1, 132.4, 134.7, 139.1, 144.3, 147.6, 154.5; IR (KBr) 3060, 2878, 1640, 1604, 1513, 1448, 1344, 1247, 1090 cm^{-1}; HRMS: m/z $[M]^+$ calcd for $C_{24}H_{18}N_2O_3$: calcd 382.1317; found 382.1316.

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